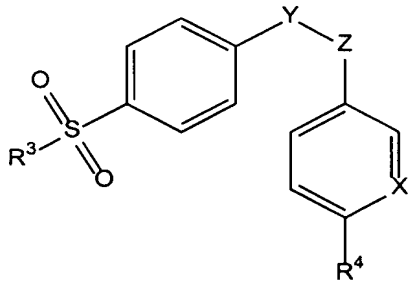
Listing of Claims

This listing of claims will replace all prior listings of claims in the application:

1. (Currently Amended) A pharmaceutical composition suitable for topical administration to an eye, the composition comprising a selective COX-2 inhibitory drug or a salt or prodrug thereof in a concentration effective for treatment and/or prophylaxis of a COX-2 mediated disorder in the eye, and at least one ophthalmically acceptable excipient ingredient that reduces the rate of removal of the composition from the eye by lacrimation such that the composition has an effective residence time in the eye of about 2 to about 24 hours, the composition being in the form of an in situ gellable solution, suspension or solution/suspension having ophthalmically compatible pH and osmolality and containing a carrageenan.

2. (Original) The composition of Claim 1 wherein the selective COX-2 inhibitory drug is of low water solubility.

3. (Original) The composition of Claim 1 wherein the selective COX-2 inhibitory drug is a compound having the formula:



where R^3 is a methyl, amino or imide group, R4 is hydrogen or a C1-4 alkyl or alkoxy group, X is N or CR5 where R5 is hydrogen or halogen, and Y and Z are independently carbon or nitrogen

atoms defining adjacent atoms of a five- to six-membered ring that is unsubstituted or substituted at one or more positions with oxo, halo, methyl or halomethyl groups; or a prodrug of such a compound.

4. (Original) The composition of Claim 3 wherein the five- to six-membered ring is a ring selected from the group consisting of: cyclopentenone, furanone, methylpyrazole, isoxazole, and pyridine ring substituted at no more than one position.

5. (Original) The composition of Claim 1 wherein the selective COX-2 inhibitory drug is selected from the group consisting of: celecoxib; deracoxib; valdecoxib; rofecoxib; etoricoxib; 2-(3,5-difluorophenyl)-3-[4-(methylsulfonyl)phenyl]-2-cyclopenten-1-one; (S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid; and 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3-(2H)-pyridazinone.

6. Canceled.

7. Canceled.

8. (Currently Amended) The composition of Claim ~~7~~1 that comprises about 0.01% to about 50% weight/volume of the selective COX-2 inhibitory drug.

9. (Currently Amended) The composition of Claim ~~7~~1 that comprises about 0.1% to about 20% weight/volume of the selective COX-2 inhibitory drug.

10. Canceled.

11. Canceled.

12. (Currently Amended) The composition of Claim ~~7~~1 that (a) comprises about 0.1% to about 6.5% by weight of one or more lightly cross-linked carboxyl-containing polymers, (b) has a pH of about 3 to about 6.5 and an initial viscosity, when administered to the eye, of about 1000 to about 30,000 cPs, and (c) gels on contact with tear fluid having a pH of about 7.2 to about 7.4.

13. (Original) The composition of Claim 12 wherein the carboxyl-containing polymer is polycarbophil.

14. (Currently Amended) The composition of Claim ~~7~~1 that comprises about 0.1% to about 2% by weight of a polysaccharide that gels when it contacts an aqueous medium having the ionic strength of tear fluid.

15. (Original) The composition of Claim 14 wherein the polysaccharide is gellan gum.

16. (Currently Amended) The composition of Claim ~~7~~1 that comprises about 0.2% to about 3% by weight of a polysaccharide that gels on contact with calcium ions, and about 1% to about 50% of a water-soluble film-forming polymer.

17. (Original) The composition of Claim 16 wherein the polysaccharide is selected from gellan gum, alginate gum, xanthan gum and chitosan.

18. (Currently Amended) The composition of Claim ~~7~~1 that comprises an ophthalmically acceptable mucoadhesive polymer.

19. (Currently Amended) The composition of Claim ~~7~~1 that is a solution or solution/suspension wherein the selective COX-2 inhibitory drug is solubilized at least in part by an ophthalmically acceptable solubilizing agent.

20. (Original) The composition of Claim 19 wherein the solubilizing agent is a cyclodextrin.

21. (Original) The composition of Claim 19 wherein the solubilizing agent is polyethylene glycol.

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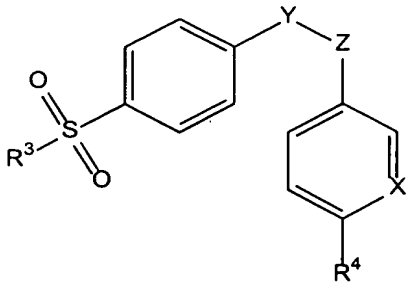
22. (Original) The composition of Claim 10 comprising from about 0.01 % to about 50 % by weight of valdecoxib, from about 0.05 % to about 10 % by weight of carrageenan, and from about 0.5 % to about 20 % by weight of hydroxypropyl β-cyclodextrin.

23. (Currently Amended) A method of treating and/or preventing a COX-2 mediated disorder in an eye of a mammalian subject, the method comprising administering in each of one or more topical applications to the eye a therapeutically or prophylactically effective amount of a composition comprising a selective COX-2 inhibitory drug or a salt or prodrug thereof and one or more ophthalmically acceptable excipient ingredients that reduces the rate of removal of the composition from the eye by lacrimation such that the composition has an effective residence time in the eye of about 2 to about 24 hours, the composition being in the form of an in situ gellable solution, suspension or solution/suspension having ophthalmically compatible pH and osmolality and containing a carrageenan.

24. (Original) The method of Claim 23 wherein the mammalian subject is a human subject.

25. (Original) The method of Claim 24 wherein the selective COX-2 inhibitory drug is a compound having the formula:



where R3 is a methyl or amino group, R4 is hydrogen or a C1-4 alkyl or alkoxy group, X is N or CR5 where R5 is hydrogen or halogen, and Y and Z are independently carbon or nitrogen atoms defining adjacent atoms of a five- to six-membered ring that is unsubstituted or substituted at one or more positions with oxo, halo, methyl or halomethyl groups; or a prodrug of such a compound.

26. (Original) The method of Claim 25 wherein the five- to six-membered ring is selected from the group consisting of: cyclopentenone, furanone, methylpyrazole, isoxazole and pyridine rings substituted at no more than one position.

27. (Original) The method of Claim 24 wherein the selective COX-2 inhibitory drug is selected from the group consisting of: celecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, 2-(3,5-difluorophenyl)-3-[4-(methylsulfonyl)phenyl]-2-cyclopenten-1-one, (S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid and 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3-(2H)-pyridazinone.

28. (Original) The method of Claim 24 that further comprises topical administration to the eye, in co-therapy, co-administration and/or co-formulation with the selective COX-2 inhibitory drug, a second drug.

29. (Original) The method of Claim 28 wherein the second drug is selected from acebutolol, aceclidine,

acetylsalicylic acid, N4 acetylsulfisoxazole, alclofenac, alprenolol; amfenac, amiloride, aminocaproic acid, p-aminoclonidine, aminozolamide, anisindione, apafant, atenolol, bacitracin, benoxaprofen, benoxinate, benzofenac, bepafant, betamethasone, betaxolol, bethanechol, bimatoprost, brimonidine, bromfenac, bromhexine, bucloxic acid, bupivacaine, butibufen, carbachol, carprofen, cephalexin, chloramphenicol, chlordiazepoxide, chlorprocaine, chlorpropamide, chlortetracycline, ciclopROFEN, cinmetacin, ciprofloxacin, clidanac, clindamycin, clonidine, clonixin, clopirac, cocaine, cromolyn, cyclopentolate, cyproheptadine, demecarium, dexamethasone, dibucaine, diclofenac, diflusinal, dipivefrin, dorzolamide, enoxacin, eperezolid, epinephrine, erythromycin, eserine, estradiol, ethacrynic acid, etidocaine, etodolac, fenbufen, fenclofenac, fenclorac, fenoprofen, fentiazac, flufenamic acid, flufenisal, flunoxaprofen, fluorocinolone, fluorometholone, flurbiprofen and esters thereof, fluticasone propionate, furaprofen, furobufen, furofenac, furosemide, gancyclovir, gentamycin, gramicidin, hexylcaine, homatropine, hydrocortisone, ibufenac, ibuprofen and esters thereof, idoxuridine, indomethacin, indoprofen, interferons, isobutylmethylxanthine, isofluorophate, isoproterenol, isoxepac, ketoprofen, ketorolac, labetolol, lactorolac, latanoprost, levo-bunolol, lidocaine, linezolid, lonazolac, loteprednol, meclofenamate, medrysone, mefenamic acid, mepivacaine, metaproterenol, methanamine, methylprednisolone, metiazinic, metoprolol, metronidazole, minopafant, miroprofen, modipafant, nabumetome, nadolol, namoxyrate, naphazoline, naproxen and esters thereof, neomycin, nepafenac, nitroglycerin, norepinephrine, norfloxacin, nupafant, olfloxacin, olopatadine, oxaprozin, oxepinac, oxyphenbutazone, oxyprenolol, oxytetracycline, penicillins, perfloxacin, phenacetin, phenazopyridine, pheniramine, phenylbutazone, phenylephrine, phenylpropanolamine, phospholine, pilocarpine, pindolol, pirazolac, piroxicam, pirprofen, polymyxin, polymyxin B,

prednisolone, prilocaine, probenecid, procaine, proparacaine, protizinic acid, rimexolone, salbutamol, scopolamine, sotalol, sulfacetamide, sulfanilic acid, sulindac, suprofen, tenoxicam, terbutaline, tetracaine, tetracycline, theophyllamine, timolol, tobramycin, tolmetin, travoprost, triamcinolone, trimethoprim, trospectomycin, isopropyl unoprostone, vancomycin, vidarabine, vitamin A, warfarin, zomepirac and pharmaceutically acceptable salts thereof.

30. (Original) The method of Claim 28 wherein the second drug is a prostaglandin.

31. (Original) The method of Claim 30 where iridial pigmentation after administration to an eye is reduced by comparison with treatment with the prostaglandin alone.

32. (Original) The method of Claim 30 where the drugs are administrated as surgical adjunct therapy in connection with eye surgery.

33. (Original) The method of Claim 30 wherein the prostaglandin is selected from latanoprost, bimatoprost travoprost and isopropyl unoprostone.

34. (Original) The method of Claim 24 wherein the composition is an in situ gellable solution, suspension or solution/suspension having ophthalmically compatible pH and osmolality.

35. (Original) The method of Claim 24 wherein the selective COX-2 inhibitory drug is present predominantly as nanoparticles.

36. (Original) The method of Claim 35 wherein average particle size of the drug is about 500 to 900 nm.

37. (Original) A method of manufacturing a medicament for topically treating or preventing a COX-2 mediated disorder in an eye, comprising a step of utilizing a composition comprising a selective COX-2 inhibitory drug or a salt or prodrug thereof and one or more ophthalmically acceptable excipient ingredients that reduce rate of removal of the composition from the eye by lacrimation such that the composition has an effective residence time in the eye of about 2 to about 24 hours in the medicament.

38. (Original) The method of Claim 23 wherein the drug is administered by electroosmosis, electroporation or by iontophoresis.

39. (Original) A pharmaceutical composition suitable for topical administration to an eye, the composition comprising nanoparticles of a drug of low water solubility in a concentration effective for treatment and/or prophylaxis of a disorder in the eye, and one or more ophthalmically acceptable excipients that reduce rate of removal of the composition from the eye by lacrimation such that the composition has an effective residence time in the eye of about 2 to about 24 hours.

40. (Original) A method of treating and/or preventing a disorder in an eye of a mammalian subject, the method comprising administering in each of one or more topical applications to the eye a therapeutically or prophylactically effective amount of a composition comprising nanoparticles of a drug of low water solubility and one or more ophthalmically acceptable excipients that reduce rate of removal of the composition from the eye by lacrimation such that the composition has an effective residence time in the eye of about 2 to about 24 hours.

41. (New) A pharmaceutical composition suitable for topical administration to an eye, the composition comprising a selective COX-2 inhibitory drug of low water solubility or a salt or prodrug thereof in a concentration effective for treatment and/or prophylaxis of a COX-2 mediated disorder in the eye, the selective COX-2 inhibitory drug being in the form of an aqueous suspension or solution/suspension having ophthalmically compatible pH and osmolality in which the selective COX-2 inhibitory drug is present predominantly in the form of nanoparticles, and at least one ophthalmically acceptable excipient ingredient that reduces the rate of removal of the composition from the eye by lacrimation such that the composition has an effective residence time in the eye of about 2 to about 24 hours.

42. (New) The composition of Claim 41, wherein the average particle size of the drug is about 500 to about 900 nm.

43. (New) A method of treating and/or preventing a COX-2 mediated disorder in an eye of a mammalian subject, the method comprising administering in each of one or more topical applications to the eye a therapeutically effective amount of a composition comprising a selective COX-2 inhibitory drug of low water solubility or a salt or prodrug thereof and one or more ophthalmically acceptable excipient ingredient that reduces the rate of removal of the composition from the eye by lacrimation such that the composition has an effective residence time in the eye of about 2 to about 24 hours, the selective COX-2 inhibitory drug being in the form of an aqueous suspension or solution/suspension having ophthalmically compatible pH and osmolality in which the selective COX-2 inhibitory drug is present predominantly in the form of nanoparticles.

44. (New) The method of Claim 43, wherein the average particle size of the drug is about 500 to about 900 nm.

45. (New) The composition of Claim 41, wherein the selective COX-2 inhibitory drug is selected from the group consisting of celecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, 2-(3,5-difluorophenyl)-3-[4-(methylsulfonyl)phenyl]-2-cyclopenten-1-one and 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3-(2H)-pyridazinone.

46. (New) The method of Claim 43, wherein the selective COX-02 inhibitory drug is selected from the group consisting of celecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, 2-(3,5-difluorophenyl)-3-[4-(methylsulfonyl)phenyl]-2-cyclopenten-1-one and 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3-(2H)-pyridazinone.